UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	13

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/292,053	Reff et al
Examiner	**Art Unit**
Marianne DiBrino	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Dec 21, 2000*

2a) [X] This action is **FINAL.** 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *38-47* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *38-47* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirem

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [X] Notice of References Cited (PTO-892)

16) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) [ ] Interview Summary (PTO-413) Paper No(s). _____

19) [ ] Notice of Informal Patent Application (PTO-152)

20) [ ] Other:

DETAILED ACTION

1. Applicant's amendment filed 12/21/00 (Paper No. 12) is acknowledged and has been entered.

Claims 38-47 are pending and are presently being examined.

The following are new grounds of rejection necessitated by the amendment filed 12/21/00.

2. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 46 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the 5E8, 6G5 and 2C8 antibodies are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the pertinent cell lines / hybridomas which produce these antibodies. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

NOTE THE CURRENT ATCC DEPOSITORY ADDRESS:
American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an

attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

Applicant may overcome this rejection by reciting specific variable region SEQ ID NOS in the claims instead of the antibody.

4. Claims 38-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating an IgE-mediated immune allergy response with anti-CD23 monoclonal antibodies (mAbs), does not reasonably provide enablement for treating or preventing any disease condition with the anti-CD23 mAbs of the instant application.

The specification does not disclose how to use the instant invention for the prevention of any autoimmune or inflammatory condition in vivo in humans. The claimed methods encompass methods of treatment of a patient suffering from any autoimmune disease or any inflammatory response. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass methods for the treatment or prevention of said diseases in vivo in humans and also encompass the same methods used prophylactically. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed compositions can be used for treatment or prevention of said diseases in humans. The specification discloses no working examples with regards to the use of the instant invention for the treatment or prevention of said diseases in vivo in humans.

The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed compositions can be used for treatment or prevention of any autoimmune disease or any inflammatory disorder. The specification discloses no working examples with regards to the use of the instant invention for the treatment or prevention of disease in vivo in humans or in animals. In addition, evidentiary reference The Merck Manual teaches that ankylosing spondylitis, which is one of the diseases disclosed on page 81 of the instant specification as being a disease preventable or treatable with the anti-CD23 antibodies of the instant invention, can be treated by NSAIDS, corticosteroids and radiotherapy to the spine. The Merck Manual does not teach any method of prevention for ankylosing spondylitis (pages 1334-1337). The Merck manual does not teach a preventive method for rheumatoid arthritis which is one of the diseases disclosed on page 83 of the instant specification as being a disease preventable or treatable with the anti-CD23 antibodies of the instant invention (pages 1305-1310).

The instant application discloses that the claimed anti-CD23 antibodies can be used to treat any disease wherein inhibition of IgE production is therapeutically desirable and (on page 81 and continuing through page 84) a multitude of disorders that allegedly can be treated by administration, including transplant rejection and including autoimmune diseases (page 83, 4th

line from bottom). There is no disclosure in the instant application for treating or preventing any disease with autoimmune or inflammatory response with the composition of the invention.

There is insufficient guidance in the specification as to how to practice the method of the instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification alone. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

Applicant's arguments in the amendment filed 12/21/00 have been fully considered, but are not persuasive.

It is Applicant's position on page 6 of the said amendment at the second full paragraph that Pater-Zyberk et al teaches amelioration of established collagen-induced arthritis by treatment with antibodies to CD23.

It is the Examiner's position that the Applicant has not provided the said reference. It is the Examiner's further position that prevention of rheumatoid arthritis is not taught by the said reference. In addition, treatment of one autoimmune disease with the antibodies of the claimed invention does not provide enablement for treatment and prevention of every autoimmune disease or inflammatory disease condition.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 46 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

> Claim 46 is indefinite in the recitation of 5E8, 6G5 and 2C8 because the recitation is of the designation for a monoclonal antibody in the absence of specific reference to a deposited hybridoma accession numbers.

Applicant's arguments in the amendment filed 12/21/00 have been fully considered, but are not persuasive.

It is Applicant's position that the instant rejection is obviated by Applicant's Sequence Listing submission of 12/21/00.

It is the Examiner's position that the instant claim 46 does not recite SEQ ID NO.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 38, 40-45 and 47 are rejected under 35 U.S.C. 102(a) as being anticipated by Bonnefoy et al (WO 96/12741) as evidenced by Saxon et al (J. Immunol. Vol. 147 (11), 1991, pp 4000-4006).

Bonnefoy et al discloses a monoclonal humanized anti-CD23 antibody with a rodent antigen binding portion and which may be either an IgG1 or an IgG3 and pharmaceutical composition thereof (especially page 4, lines 1-3 and lines 15-19, page 5, lines 4-11 and 25-27 and claims 11-15) and a method for treating allergic diseases using said antibody, including blocking an IgE immune response (especially page 8, lines 20-22 and claims 1-4). It is an inherent property of anti-CD23 antibodies to inhibit IgE expression (IL-4 induced) as evidenced by Saxon et al (especially Abstract and page 4004, column 1). The instant claims are included in this rejection because the ability to inhibit IgE expression in vivo is an inherent property of said antibodies because they have this property in vitro.

The reference teachings anticipate the claimed invention.

Applicant's arguments in the amendment filed 12/21/00 have been fully considered, but are not persuasive.

It is the Applicant's position on page 8 of the said amendment at the last two paragraphs and continuing on to page 9 at the first two paragraphs, that Bonnefoy et al does not disclose an anti-human CD23 mAb comprising a human gamma-1 constant region. It is the Applicant's further position that there is no indication of therapeutic enhancements obtained in conjunction with providing an antibody including a human gamma-1 constant region, and the said reference fails to recognize the advantages of employing a human gamma-1 constant region in connection with the therapeutic and phrophylaxis methods of the invention.

It is the Examiner's position that the reference teaches anti-CD23 monoclonal antibodies that have a human IgG1 constant region and a method for treating allergic diseases using the said antibodies, including blocking IgE immune response. It is not necessary that Bonnefoy et al recognize the therapeutic enhancements obtained in conjunction with providing an antibody including a human gamma-1 constant region.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 38-45 and 47 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bonnefoy et al (WO 96/12741, Applicant's IDS reference) in view of Saxon et al (J. Immunol. Vol. 147 (11), 1991, pp 4000-4006, Applicant's IDS reference) and Newman et al (U.S. Patent No. 5,658, 570).

Bonnefoy et al discloses a monoclonal humanized anti-CD23 antibody with a rodent antigen binding portion and which may be either an IgG1 or an IgG3 and pharmaceutical composition thereof (especially page 4, lines 1-3 and lines 15-19, page 5, lines 4-11 and 25-27 and claims 11-15) and a method for treating allergic disease using said antibody, including blocking an IgE immune response (especially page 8, lines 20-22 and claims 1-4).

Bonnefoy et al do not disclose a method of treating an allergic disease using an anti-CD23 antibody comprising a primate antigen binding region.

Saxon et al teach that anti-CD23 antibodies inhibit IgE expression (especially Abstract).

Newman et al disclose chimeric or humanized anti-CD23 antibodies which comprise a human constant region of IgG isotype and a primate antigen binding region (especially claims 1-8 and column 8, lines 52-53) and a method of administering a therapeutically effective amount of said antibody (especially also column 6, lines 1-8) . Newman et al also disclose that non-human primate antibodies are expected to be an improvement over mouse monoclonal antibodies for in vivo human therapy (especially column 1, lines 45-51). Newman et al further disclose that chimeric mouse-human antibodies elicit antibody production when used in humans (especially column 1, lines 40-44).

It would have been prima facie obvious at the time the invention was made to have used the anti-CD23 antibody of Newman et al in the method of Bonnefoy et al. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to treat an allergic disorder in a human with reduced side effects from immunogenicity of the anti-CD23 antibody. Claim 33 is included because the ability to inhibit IgE expression in vivo is an expected property of said antibodies because they have this property in

Applicant's arguments in the amendment filed 12/21/00 have been fully considered, but are not persuasive.

The basis for Applicant's arguments for Bonnefoy et al discussed supra applies here. It is Applicant's further position (beginning on page 9 third paragraph of the said amendment) that the references alone or in combination do not indicate the potential benefit of the incorporation of a human gamma 1 constant domain on the ability of a particular antibody to human CD23 to inhibit IgE production. It is also Applicant's position (beginning on the last two lines of page 10 of the said amendment) that the inventors have surprisingly discovered that the human gamma 1 containing anti-human CD23 antibodies of the present invention possess substantially better activity than an otherwise identical anti-human CD23 antibody containing a human gamma 4 constant domain, and the Applicant's cite page 17 of the instant specification.

It is the Examiner's further position that Bonnefoy et al teach anti-CD23 antibodies in pharmaceutical compositions, and that the human constant domains of such antibodies elicit a negligible immune response when administered to a human compared to the immune response mounted by a human against a rat or mouse antibody (page 5 at lines 4-11, these lines cited in the last Office Action), a substantial reason to produce such a chimeric antibody. It is not necessary that the inhibiting activity of anti-CD23 antibodies be correlated to the presence or absence of particular human constant domains.

It is the Applicant's position that the inventors have surprisingly discovered that the presence of human constant domains correlates to "better activity" (the Examiner presumes to IgE inhibition), and Applicant points to page 17 of the specification. In the specification, it is Applicant's position that antibodies with a γ1 constant region is superior to the primate antibodies or to chimeric antibodies with an γ4 human constant region in the inhibition of IL-4 induced IgE expression.

It is the Examiner's position that the two primate antibodies disclosed and discussed on pages 17-18 of the instant specification are 5E8 and 6G5, and data for these antibodies and their primatized, i.e., chimeric human constant region, γ1 and γ4 containing, counterparts are disclosed in Figures 3 and 5 and in the Brief Description of the Drawings for the said figures. In the instance of the 6G5 series of antibodies shown in Figure 5, the primate antibody (6G5) , and the primatized antibodies with either the γ1 (6G5G1) or γ4 (6G5G4) human constant

regions perform the same at all three concentrations of antibody in the inhibition of production of IL-4 induced IgE expression, noting the standard error bars. In the instance of the 5E8 series of antibodies shown in Figure 3, the primatized antibodies with the γ1 human constant region (5E8G1 and 5E8G1N) perform comparably to the primatized antibodies with the γ4 human constant region (5E8G4P and 5E8G4PN) at the lowest concentrations of antibody and one (5E8G4P) performs perhaps slightly better at the highest concentration of antibody, noting the standard error bars.

11. Claim 46 appears to be free of the prior art.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is (703) 308-0061. The examiner can normally be reached Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
May 25, 2001

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP ~~1800~~ 1600